

Serial No: 09/526,193
Filed: 15 March 2000

COMPLETE PENDING CLAIM SET

135. (Twice Amended) A process for identifying a compound that modulates mammalian ABC1 (ABC1) polypeptide biological activity comprising contacting a compound with a human ABC1 polypeptide that has ABC1 biological activity and in the presence of adenosine triphosphate (ATP) under conditions promoting the biological activity of said ABC1 polypeptide and detecting a difference in said biological activity following said contacting relative to when said compound is not present
wherein said biological activity is binding or hydrolysis of adenosine triphosphate (ATP) and wherein said human ABC1 (hABC1) comprises amino acids 1-60 of SEQ ID NO: 1,
thereby identifying an ABC1 modulating agent.

136. (Amended) The process of claim 135 wherein said difference in biological activity is an increase in biological activity.

142. (Amended) The process of claim 135 wherein said human ABC1 (hABC1) comprises the amino acid sequence of SEQ ID NO: 1.

143. (Twice Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity comprising contacting a compound with a membrane comprising a mammalian ABC1 polypeptide, in the presence of a lipid under conditions promoting transport of said lipid across said membrane, wherein said lipid is phospholipid or cholesterol, and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

144. (Amended) The process of claim 143 further comprising contact with an acceptor that accepts the transported lipid, said acceptor being a member selected from

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the group consisting of phospholipid, high density lipoprotein (HDL), Apolipoprotein (Apo) AI, ApoAI and ApoE.

145. (Amended) The process of claim 143 wherein said compound is useful in treating coronary artery disease (CAD). R

148. The process of claim 143 wherein said membrane is part of an intact cell. L R

149. (Amended) The process of claim 148 wherein said cell is a fibroblast or a macrophage. R

151. The process of claim 148 wherein said cell is a recombinant cell. ✓ R

156. The process of claim 143 wherein said transport is cholesterol efflux. ✓ R

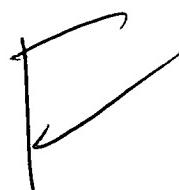
157. The process of claim 143 wherein said mammalian ABC1 is mouse ABC1. ✓ R

158. (Amended) The process of claim 143 wherein said mammalian ABC1 is human ABC1. R

159. (Amended) The process of claim 158 wherein said human ABC1 comprises amino acid residues 1-60 of SEQ ID NO: 1. R

160. (Amended) The process of claim 158 wherein said human ABC1 comprises the amino acid sequence of SEQ ID NO: 1. R

161. (Twice Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity and is useful in modulating plasma cholesterol levels in a mammal comprising contacting a compound with a membrane comprising a human ABC1 polypeptide, wherein said polypeptide comprises amino acid



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residues 1-60 of SEQ ID NO: 1, and a source of one or more anions under conditions promoting transport of said one or more anions across said membrane and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

162. (Amended) The process of claim 161 wherein said difference in anion transport is an increase in said transport.

163. (Amended) The process of claim 161 wherein when said one or more anions comprises at least two different anions.

165. (Twice Amended) The process of claim 161 wherein said human ABC1 comprises the amino acid sequence of SEQ ID NO: 1.

166. (Twice Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity for use in treating CAD comprising contacting a compound with a membrane comprising a human ABC1 polypeptide and interleukin-1 under conditions promoting transport of said interleukin-1 across said membrane and detecting a difference in said transport following said contacting relative to when said compound is not present and wherein said human ABC1 comprises amino acids 1-60 of SEQ ID NO: 1, thereby identifying a mammalian ABC1 modulating agent useful for treating CAD.

168. (Amended) The process of claim 167 wherein said human ABC1 comprises the amino acid sequence of SEQ ID NO: 1.

169. (Amended) A process for identifying a compound that modulates mammalian ABC1 protein biological activity and is useful in modulating human plasma cholesterol levels comprising contacting a compound with a human ABC1 protein that has ABC1 biological activity and in the presence of a protein that binds to said human

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ABC1 protein under conditions promoting binding of said protein to said ABC1 polypeptide, wherein said human ABC1 protein comprises amino acids 1-60 of SEQ ID NO: 1, and detecting a difference in said binding following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

172. (Amended) The process of claim 169 membrane is part of an intact cell. ✓ R

173. (Amended) The process of claim 172 wherein said cell is a recombinant cell. R

174. (Amended) The process of claim 161 wherein said membrane is part of an intact cell. ✓ R

175. (Amended) The process of claim 166 wherein said membrane is part of an intact cell. ✓ R

176. (Amended) A process for identifying a compound that modulates mutant human ABC1 (hABC1) polypeptide biological activity comprising contacting a compound with a mutant hABC1 polypeptide, comprising from 1 to 5 amino acid differences relative to the sequence of SEQ ID NO: 1, and a member selected from the group consisting of a lipid, a protein, ATP, and interleukin-1, and detecting a difference in said biological activity following said contacting relative to when said compound is not present thereby identifying a mutant hABC1 modulating agent. ✓ R

178. The process of claim 176 wherein said mutant hABC1 polypeptide comprises a single amino acid difference relative to the sequence of SEQ ID NO: 1. ✓ R

179. (Amended) The process of claim 143 wherein said hABC1 comprises a detectable label. ✓ R

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180. The process of claim 179 wherein said label is a fluorescent label. ✓ R

181. (Amended) The process of claims 143 wherein said ABC1 polypeptide is a recombinant polypeptide. ✓ R

184. (Amended) A process for identifying a compound that modulates cholesterol levels in a mammal comprising administering to said mammal an effective amount of a compound that has ABC1 modulating activity in the process of claim 143 and determining a difference in cholesterol level in said mammal following said thereby identifying a compound that modulates cholesterol levels in a mammal. W

185. The process of claim 184 wherein said difference in cholesterol level is a decrease in plasma cholesterol level. W

186. The process of claim 184 wherein said difference in cholesterol level is an increase in plasma HDL-cholesterol level. ✓ W

188. (Amended) The process of claim 182 wherein said mammal is a human. W

189. (Amended) A process for identifying a compound that modulates ABC1 expression comprising contacting a compound with a cell that expresses a polynucleotide construct, said construct comprising a mammalian ABC1 promoter operably linked to a reporter gene, under conditions promoting expression of said reporter gene and detecting a difference in said expression in the presence of said compound relative to when said compound is not present, wherein said expression is synthesis of mRNA or protein, thereby identifying a compound that modulates ABC1 expression. W

190. The process of claim 189 wherein said difference in expression is an increase in expression. ✓

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192. The process of claim 189 wherein said cell is a recombinant cell. *w*

193. (Amended) The process of claim 189 wherein said cell is a fibroblast or a macrophage. *w*

194. (Amended) The process of claim 189 wherein said promoter is the promoter found in BAC RPCI -11 317. *w*

Please add the following new claims:

213. (New) A process for identifying a compound that modulates lipid transport across a mammalian cell membrane that includes ABC1 polypeptide, comprising testing a mammalian cell that includes in the cell a lipid selected from the group consisting of phospholipid and cholesterol, under conditions promoting transport of said lipid across said membrane, and comparing transport of said lipid in the presence and absence of a test compound whereby a difference in said transport indicates modulation, thereby identifying said compound as a modulator of lipid transport. *R*

214. (New) The process of claim 213 wherein said modulation is an increase in lipid transport. *R*

215. (New) The process of claim 213 wherein said modulation is a decrease in lipid transport. *R*

216. (New) The process of claim 213 wherein said mammalian cell is a fibroblast. *R*

217. (New) The process of claim 213 wherein said mammalian cell is a mouse cell. *R*

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218 (New) The process of claim 213 wherein said mammalian cell is a human R cell.

219. (New) The process of claim 213 wherein when said lipid is a phospholipid. R

220. (New) The process of claim 213 wherein when said lipid is cholesterol. R

221. (New) The process of claim 213 further comprising the presence of an acceptor that accepts the transported lipid, said acceptor being a member selected from the group consisting of phospholipid, high density lipoprotein (HDL), Apolipoprotein (Apo) AI, ApoAI and ApoE. R

222. (New) The process of claim 221 wherein said acceptor is HDL. R

223. (New) The process of claim 213 wherein said mammalian cell is a recombinant cell. R

224. (New) The process of claim 143 wherein said modulation is an increase in transport. R

225. (New) The process of claim 143 wherein said modulation is a decrease in transport. R